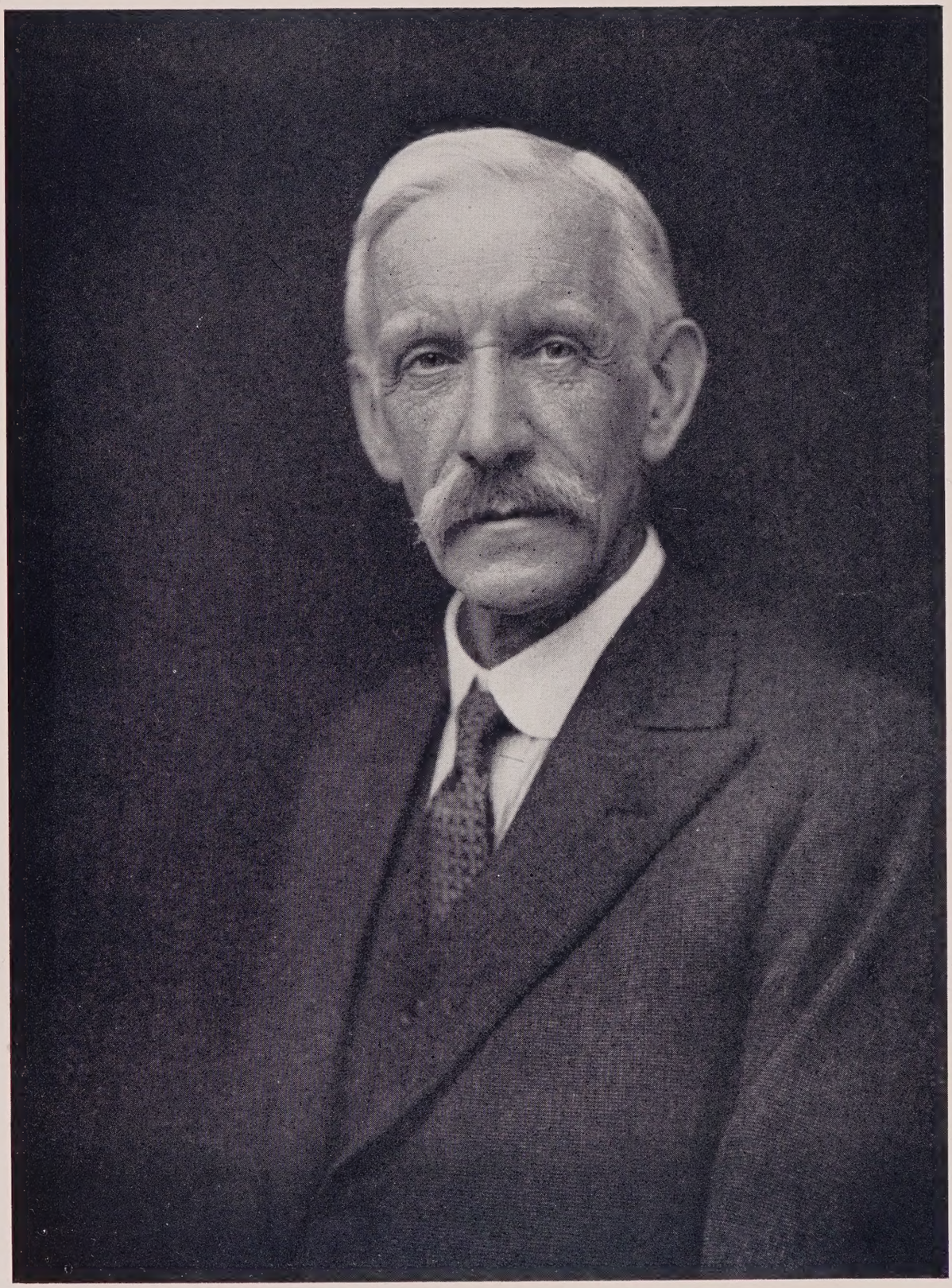
pam (B) 1Hop

FREDERICK GOWLAND HOPKINS

1861—1947

pam (B) / HOP



T. S. Hopkins

[Reprinted without change of pagination from *Obituary Notices of Fellows of The Royal Society*, Volume 6, November 1948]

FREDERICK GOWLAND HOPKINS

WELLCOME LIBRARY INSTITUTE

1861–1947

Parentage and Ancestry

Frederick Gowland Hopkins was born in 1861 at Eastbourne, whither his parents had moved on their marriage. His paternal great-grandfather was a Captain Hopkins, R.N., who, according to family tradition, commanded a ship at Trafalgar. The Captain is said to have had a large family, and some of the sons, including our subject's grandfather, went into business in London. Two other members of this family deserve special mention. One of them, Manley Hopkins, became Consul-General for the Hawaiian Islands to Great Britain, and his eldest son was Gerard Manley Hopkins, the Jesuit poet. According to the biographer of the latter, G. F. Lahey, S.J., the father was also a man of high intellectual endowment and something of a poet. Hopkins could remember that, as a boy, he was taken by his mother to visit the family of Manley Hopkins, uncle of his late father, and that the son Gerard, the poet, was present, though he did not recall him very clearly from that memory of childhood. The other member of the Captain's family to be mentioned, as having through her descendants made contact with our subject's life and career, is Louisa, who married Johann Leopold Abel, a German by birth. Among the offspring of this marriage was Frederick Augustus Abel (later Sir Frederick Abel, Bt.), who became eminent as a chemist and, in particular, an authority on the chemistry of explosives. He did important work for the British Government in that field, was elected F.R.S. in 1860 and was a close friend of his cousin, our Hopkins's father. A younger brother of Frederick Abel became, through a daughter, the grandfather of Carl Frederick Abel Pantin, F.R.S., who was to be a colleague of Hopkins, as a Fellow of Trinity College, Cambridge.

To return to the direct line of ancestry, Hopkins's paternal grandfather settled in Bishopsgate Street, in the City of London, as a bookseller and an occasional publisher, and there his son, Hopkins's father, was born and educated, entered business and continued to live until he married. Hopkins's grandparents on his mother's side came both from Sunderland, the grandmother being of a family named Stafford, well known and influential locally in the world of shipping, while the grandfather, Gowland by name, was a jeweller in the retail business. Hopkins had been told, no doubt by his mother, that the Stafford family frowned upon the connexion, and severed all relations with the young couple when they made a runaway marriage. They also settled in the City of London, in Leadenhall Street; and there, too, Hopkins's mother was born and lived till she was married. He found some pleasure in this tale of his grand-

parents' elopement, as lending a touch of romance to the family history on that side; and indeed, if we may judge from the attitude which was later to have a decisive influence on the course of his own education, not much of this spirit of romantic enterprise would appear to have been transmitted to his mother's generation.

Childhood and Schooling

Hopkins's parents, who thus had both been born and lived for many years in the City, went on their marriage to live in Eastbourne, where he was born; but while he was still an infant his father died, and he had no living memory of him. Gradually, however, during his boyhood and later, he gathered details from which he could construct an imaginative picture of him, which may well have had an early influence on his own interests and inclinations. This portrait of his father, though not clear at all points, gives an impression of ability and charm. There was abundant evidence of the affectionate regard in which he had been held by a wide circle. In those days, when London offered very little of commercially organized entertainment for the leisure hours of its City men, and when many still lived at or near their places of business, keen followers of science were certainly to be found among them in much higher proportion than among their successors to-day. There was then in the City a 'Scientific and Literary Society' for such amateurs, informal in its constitution but with a very large membership; and of this Society Hopkins's father had been President for some years before his marriage. Among the papers and diaries which he left were notes for addresses to be given, abstracts from scientific literature and other such indications of the direction and range of his reading and his interests. His most intimate friend, as mentioned, was his cousin, Frederick Abel, already holding a position of distinction among professional scientists. There is, of course, no reason to think that the scientific attainments of Hopkins's father were much above the general level of those of his friends and associates among the amateurs, or that they would have become notable if his life had been extended to the normal span; but such record as he left of his activities makes it reasonable to suppose that he would have been both eager and well qualified to recognize the special direction of his child's genius and to make appropriate plans for an education which, lacking his guidance, was to fall into a devious and abnormal course.

After her husband's death Hopkins's mother continued to live in Eastbourne, and there, for the next ten years, he was to pass with her a childhood of unusual loneliness. The house where they lived, Cavendish House, was directly opposite to the site of the pier, and the first stages in the construction of this provided Hopkins with some of his earliest memories, his notes of which seem to awaken echoes from a world of Dickens and Tom Hood. He remembered seeing the first iron pillar of the pier screwed into the socket of its base. The motive power was supplied by a wooden capstan-head, with six walking coastguards to push the spokes, while another with a tarred straw hat was perched on the rotating top of it and encouraged their efforts by playing a fiddle. The sight made a deep

impression on the little boy, who, like many another such, decided then to be an engineer. Looking back through the years, however, Hopkins thought that he had shown less mechanical ability than most boys, and that throughout his life, indeed, in spite of all the experience and the demands of work in laboratories, his manual skill in construction remained below the average. So far as he retained a clear memory of his own early doings and interests, these were such as to suggest literary rather than scientific aptitudes. He seems to have been rather a bookish child, reading Dickens before he was ten years old, and becoming adept at writting doggerel rhymes; and in the latter connexion it may be recalled that when, late in life, he acquired a University institute of his own, and his colleagues and research students published a journal to take the overflow of departmental high spirits, it gave the Professor no trouble to contribute, on occasion, verse of the appropriate tone and level. Not till he was eight or nine years old did the little Hopkins make a first, distant contact with the natural sciences, which had occupied much of the leisure of the father he had not known. It was then that his mother first allowed him to have a limited use of a good microscope and an astronomical telescope of some kind, which had been left by his father. The telescope was evidently not of much account, and its use to any purpose would have been beyond the scope of an unguided child; but the microscope, with access to a varied wealth of material from the sea-shore, gave him, even without help, a first glimpse into a new world of interests. In after years he recalled the feeling which it aroused, of something immensely more important than what he was learning at school; but there was nobody to share the experience with him, or to guide him, as his father could have done, to some understanding of what he saw.

His mother, affectionate and devoted, knew nothing of such things, and her duty to his education was fulfilled by sending him as a day-boy, when he was six years old and for the remainder of their stay at Eastbourne, to a school kept by two ladies. His memory of the teaching there was favourable; but the discovery of a case of cruel bullying among the boarders, shortly before he left, seems to have left a scar on his young mind, and to have made him unduly sensitive and introspective for years afterwards. In 1871 his mother left Eastbourne with him for Enfield, to live with her mother and an unmarried brother, a business man who built a house there, in what was then pleasant country on the London outskirts. This was to be Hopkins's home for more than twenty years. At the age of ten and a half years he was sent to the City of London School, the headmaster being then Dr Abbott. Starting in the lowest form he made normal progress up the school for three years. Towards the end of that period, having had classes in the subject with one Henry Durham, whom he remembered as an excellent teacher, he took a school examination in Chemistry, and found himself one of three placed in the first class, the other two being the brothers W. H. and A. G. Perkin, both to become pre-eminent in their own different fields of organic chemistry. In the next term he was awarded the prize of his class for English and another for the best 'essay', which appears to have been a rendering of the plot of Scott's *Old Mortality* into blank verse.

Hopkins himself was led to speculate, later in life, on the possible effect of these successes on his career, if he had stayed at the school to receive the prizes, and thus to be brought to Abbott's notice. He had shown very early, as we have seen, some literary inclination; and he retained, indeed, through life a natural aptitude for the vivid and effective use of language, to which his scientific papers and addresses bear witness. Notice from such a headmaster as Abbott would surely have brought encouragement, which later contact with the efficient teachers of the upper forms would have reinforced, for a boy showing that kind of promise to follow the then conventional path of classical scholarship to a university. Even so, if his other childish enthusiasm, for natural science, had survived and had then prevailed, he might well have found the opportunity to embark upon his life's work much earlier, and in a form very different from that in which it was to come to him, many years later, after a training both varied and unacademic. What happened was that, for no reason that he was ever able to make clear to himself, he just stayed away from school one day, and then, shrinking from the inevitable inquiry and confession if he returned, persisted in the truancy for the weeks still to run before the term ended. So far as memory could find any reason for the escapade, he thought that it was due simply to boredom and loneliness, to which the long daily journey to and fro, and a natural shyness, deepened by his secluded home life and memory of the bullying incident, all made their contributions. One pictures him as a small and rather bewildered unit in a crowd; he himself records, surprisingly, that he had never, in over three years at the school, received a personal word from any of the masters, until discovery led, at the end, to a terrifying and humiliating interview with Abbott himself. Meanwhile he had spent his stolen days in country walks, and in visits to museums, a public library and, on occasion, the London docks, without any lapse into positive mischief. It is even credible that his keen young intelligence might, for a few weeks, have been more usefully employed in these explorations than it would have been in school. The delinquency, however, was not one to be passed over, and, though he was not formally expelled, his 'removal was advised'. So, at fourteen, he had to make a fresh start at a private school, where he remained for the next three years. The teaching there seems to have been of a trivial order; Science, as he remembered it, was represented by occasional readings from Huxley's *Elementary Physiology*—in which the headmaster appears to have found texts for discourse on design in creation—and a chemical laboratory which was never used. Nevertheless Hopkins, being entered for an examination of the College of Preceptors, won a prize for science ; and, in spite of its rather gross defects on the formal side of education, the years at this school seem at least to have given him self-confidence and enabled him to make friends.

City Clerk and Analyst's Assistant

Thus, at the age of seventeen, Hopkins finally left school and his education was thought, by his family, to be complete. The determination of his future

career lay with his uncle, who had no idea but to find for him a suitable opening into business in the City. This was presented, through the influence of a family friend, in the form of a clerk's stool in the office of an Insurance Company. After he had occupied this for six months, however, the same friend, for no recorded reason but certainly with discernment, thought better of his recommendation. He now suggested that Hopkins should be given a chance to make more immediate use of his brains, and even offered the opinion that he seemed to be more fitted for a scientific career. This was certainly in line with his own ideas, and, on the advice of his father's cousin and special friend, Frederick Abel, a decision was actually taken then to send him to Cambridge. There was no serious financial hindrance, and a path seemed now to be open, by following which he might, after all, have been able to enter upon his life's work for science at a normal age. Again, however, the opportunity was allowed to pass, but this time through no fault of his own. His uncle, a business man with no experience of university education and no conviction of its value, met a City acquaintance who, by his connexion with a pharmaceutical firm, was thought to be qualified to give sound advice on such a matter. He took the view that practical knowledge, required to make a living out of science, could only be obtained in the laboratory of a practising analyst; and, as it happened, he knew a consulting chemist in the City who had a vacancy for an articled pupil. This advice was accepted, and Hopkins spent the next three years in activities which were supposed to qualify him for such a career. The experience, as he recalled it, was unsatisfying and unpleasant. The articled pupils had, indeed, the opportunity of learning from an assistant, on purely empirical lines, such conventional analytical methods and tests as were required to deal with the variety of problems which came to the laboratory; but after a few months of such training they became, in effect, additional assistants, kept hard at work daily from 9 a.m. to 6 p.m. without any remuneration; on the contrary, they had paid handsomely for the privilege. They received no instruction outside the practical needs of the moment, and the long hours of work, with long journeys at both ends, left the young Hopkins with little time or energy for study on his own account. But although, in retrospect, he found so little for satisfaction in this interlude, it may be permissible to suspect that he really gained more than he recognized, from the manipulative dexterity and the instinct of the skilled analyst which he acquired during these three years of hard and rather sordid employment in a consultant's laboratory.

When they came to an end, his further course remained open for decision; and having now received a small inheritance on the death of his paternal grandfather, he was free to choose for himself. He was still only twenty years of age, and Frederick Abel again advised Cambridge; but Hopkins seems to have decided on his own account that it was now too late for that, and that he had better take a course in chemistry at the Royal School of Mines at South Kensington, where Edward Frankland was then the famous Professor. Some reorganization then in progress seems to have kept Professor Frankland away from the laboratory and even from the lecture theatre for most of that term; but Hopkins did well in the examination at its end, and was at once invited by

the professor's son, Dr Percy Frankland, only three years his senior, to become his assistant in a private laboratory. There he found himself again engaged on analyses, chiefly of creosote and steel samples for a railway. Again, however, it was merely an interlude, and in this case a short one; for after about six months the work for the railway came to an end, and Hopkins, deciding now to prepare himself for the Fellowship of the Institute of Chemistry, then in its early years, became a student at University College, London, where he joined Charles Graham's class on technical chemistry. Graham's teaching, it would appear, had little to give him, beyond what he had already acquired in his years of mixed experience as an analyst; and he had begun to crave the opportunity, not yet in sight, to make contact with chemistry as a fundamental science, whereas his attention, hitherto, had been concentrated on issues no deeper than immediate and practical applications.

Forensic Medicine and Graduation

The opportunity was on the way, however, and with it his first real foothold on the scientific ladder, when he presented himself as a candidate for the Associateship of the Institute of Chemistry. He must have done remarkably well in the examination; indeed, in spite of the unusual character of his preparation for most of them, examinations, as such, seem never to have caused him much trouble. In this case his success was such as to bring him to the notice of Dr (later Sir Thomas) Stevenson, who was the principal analyst and expert witness then retained by the Home Office in prosecutions for poisoning, as well as the Lecturer on Forensic Medicine at Guy's Hospital, where he had his laboratory. Stevenson offered Hopkins a position as his assistant, which was eagerly accepted; and thus, at the age of twenty-two, he entered upon five years of an appointment which gave him work which interested him, under a congenial and considerate chief, and, what was of more importance for his future, a certain margin of leisure to begin to follow his own ideas and, so far as he could do this by his own effort, to fill gaps in his equipment of formal education and academic credentials. And even more important than either of these, perhaps, was the chance which came of contacts with men of ability and rising influence in Guy's Hospital and its Medical School. He was concerned with Stevenson in investigations required by a number of cases in the Courts, including some famous trials for murder by poisoning—by aconite in the Lamson case, arsenic in the Maybrick case, chloroform in the Bartlett case and nitric acid (mixed, as Hopkins discovered, with sulphuric acid) in the Lipski case. Meanwhile he had formed a close friendship with John Wade, later to become Lecturer on Chemistry at Guy's Hospital Medical School, who, like Hopkins, had yet no university degree. They decided together that, by study in spare time, they would prepare themselves for the examinations of the University of London leading to the B.Sc. degree. Both had to start from the beginning, with matriculation, and this, for Hopkins especially, must have presented a formidable hurdle; for six years had now elapsed since his inefficient schooling

in its subjects had come to an end. And now he had to begin these again and to bring himself up to matriculation standard by self-tuition, finding time for this on his daily journeys between Enfield and Southwark, in evenings much broken by family claims and during his short holidays. There was no check, however, and both he and Wade achieved graduation in the shortest possible time. The only help they had required was from a class in practical biology at Birkbeck College, which they kept in grateful memory.

Student of Medicine and Research Student at Guy's Hospital

Hopkins was later doubtful concerning the ultimate effects of this course of self-inflicted cramming, extending over three years. The attainment of its object, however, emboldened him to make another and most important decision. In 1888, being now in his twenty-eighth year, he entered Guy's Medical School as a student, having been encouraged to take this step by Sir Thomas Stevenson, who thought that, with a medical degree, Hopkins might eventually succeed him. When Stevenson died, Hopkins, then established already for some years at Cambridge, did, in fact, accept appointment as an analyst and expert adviser to the Home Office on a part-time and occasional basis, but only for a few years.

The reputation of Hopkins's special qualities had evidently spread already beyond Stevenson's laboratory; for, on joining the School as a medical student, he received immediately the first award of a research studentship which had been founded in memory of Sir William Gull, and the tenure of this gave him some standing and privileges with the hospital staff. And now, for the first time in his chequered experience, he heard lectures of a university standard, on the subjects required for the Intermediate M.B. of London University. These were not, however, of a character to leave a lasting impression; for those on physiology at Guy's were still being given by one of the physicians, and Starling's appointment on a whole-time basis was not made till some years later. Hopkins, however, according to his custom, passed the examination without difficulty and even with distinction. He was himself aware, though not proud, of his natural facility, which practice had perhaps developed by this time, for rapidly memorizing material required in an examination and forgetting it almost as quickly. On his performance in this Intermediate M.B. examination he was awarded the gold medal in chemistry and honours in materia medica. According to his own account, his knowledge of the latter subject was entirely the result of cramming from Hale White's textbook for two days before he took the paper on it, and soon evaporated; but it should be noted that, years afterwards, when Hale White had become one of his closest friends, he was to write an introduction to a later edition of that book, full of constructive and suggestive ideas towards the laying of a truly scientific foundation for therapeutics. Of more serious concern for later demands on him at Cambridge was an experience, by no means peculiar to him, that the details of descriptive anatomy, acquired at the cost of many strenuous hours in study and dissecting room, faded from his memory as soon as they had been used to satisfy the examiners.

Uric Acid

Hopkins's clinical studies at Guy's were eased and made pleasant by the consideration of the members of the Hospital Staff, who recognized that his tenure of the studentship gave him duties outside their wards. In some cases they further encouraged him to embark on investigations arising from study of their cases; and though these led directly to nothing of importance, in one instance at least there was a valuable incidental outcome, in the method for determining uric acid in urine, which Hopkins published in the *Guy's Hospital Reports* in 1891, and in the *Proceedings of the Royal Society* in 1893, while he still held the Gull Studentship. This was, in fact, his first serious scientific publication, and his method remained the standard one for many years, until more convenient colorimetric ones were introduced; and it may be suggested that his long preliminary experience of analytical methods must have had some connexion with the firmness of this, the first step into the main field of his life's work, biochemistry, taken when he was already thirty years old. Uric acid, which then figured more prominently in medical speculations than in more recent times, continued to occupy Hopkins's attention for some years, and, in 1898, he published with W. B. Hope the results of an investigation on its occurrence in relation to diet, showing that the rise observed after food was not to be accounted for wholly by the intake of nucleins. It seems clear also that his frequent dealings with uric acid in this period helped to turn his attention to a problem of insect metabolism, and thus led to his second important contribution to biochemistry.

Butterfly Pigments

We have seen that Hopkins had very early in life given promise of an interest in natural history, and evidence that this had grown with the years of his boyhood is to be found in a communication by him which was published in the journal, *The Entomologist*, in November 1878, just after he had left school at the age of seventeen. The note describes the unusual abundance during that year of the little bombardier beetle, *Brachinus crepitans*, which he had found in numbers near his home at Enfield and also on the South Downs near Eastbourne. It further records the complete absence, near his home in that year, of *Colias edusa*, the clouded-yellow butterfly. Fifty-seven years later, in an address to the London Natural History Society, given on the occasion of his election as its Honorary President in succession to Earl Grey of Falloden, Hopkins revealed in retrospect what had probably been the main source of the interest which, as a boy, he had taken in the bombardier beetle.

> 'It was plentiful that year,' he said, 'and I found it in a northern suburb of London and on the South Downs near Eastbourne. Now, when one day I beheld, without previous knowledge of their abilities, how these insects on being disturbed eject a violet vapour into the air, a most effective act for offence or defence, I felt an intense curiosity to know not only how this volatile

stuff could be made and stored but in particular what the stuff could be. I tried a few experiments, putting one bombardier after another into the same test-tube and encouraging each to shoot. The vapour condensed on the side of the covered tube and I thus collected a little of the material. It was very little, however, and I was a youth with no chemical training, so nothing came of my researches. I think, however, that from that time my fate was sealed. Though the designation was not yet invented, I became there and then a biochemist at heart.'

At Guy's Hospital, soon after he became a medical student and received the Gull award, he began to find a link between this earlier curiosity about the chemical products of insects and the new interest in uric acid, to which he had been led by problems in the wards. Throughout his life he repeatedly showed an instinctive recognition of connexions which others had missed, and a few experiments convinced him of the close relation to uric acid of the white and yellow pigments in the wing-scales of a large family of butterflies, the *Pieridae*, including the cabbage-white, brimstone, clouded-yellow and many other species. A preliminary communication on these pigments was made to the Chemical Society in 1889, but it was not till 1895 that the full paper was ready. He sent it for an opinion to Ray Lankester, who at once communicated it to the Royal Society for publication in the *Philosophical Transactions*. Hopkins had reached the conclusion that the white pigment, soluble in alkaline water and reprecipitated on neutralization, was uric acid, which it also resembled in its crystallization and in giving the murexide test. The yellow pigment, readily soluble in hot pure water and precipitated on cooling, he identified with a substance originally described by Wöhler, as obtained, together with ammonium urate, by prolonged heating of uric acid with water in a sealed tube. Hopkins repeated the preparation, separating the yellow product more completely than others had done and showing its close resemblance, in many respects, to the natural yellow pigment from the Pierids. He proposed to call the substance 'lepidotic acid', and found it, with uric acid, in the material which, in these species, collects in the rectum of the pupa and is extruded by the imago on its emergence. The yellow pigment, both natural and artificial, gave on prolonged boiling with acids a dark red substance, soluble in strong sulphuric acid but in hardly any other solvent, to which Hopkins gave the name Lepidoporphyrin. The name was hardly appropriate, for, in spite of similarities in colour and behaviour, there is no ground now for suspecting that this substance has any structural connexion with the true porphyrins. Hopkins, however, must have retained especially happy memories of this early adventure into insect biochemistry, for, when his portrait came to be painted for the Royal Society in 1938, and the artist, Mr Meredith Frampton, posed him at the laboratory bench with his hand writing on a pad of paper, the word which he wrote, and which is clearly to be read in the picture, was Lepidoporphyrin. Reading the paper in *Phil. Trans.* to-day, one seems to partake of the joy of a discoverer reporting the success of his first major enterprise in research. To those who

read it when it appeared, it may well have signalled the rise of a new star of first magnitude in the sky of research, so novel and convincing are the data, and so orderly the presentation. It remains still the achievement of a pioneer, though the chemical identifications, which it seemed to make with such precision and elegance, have not held good. Many years afterwards the researches of Wieland, Schöpf and their co-workers were to replace the uric and lepidotic acids of Hopkins's account by leucopterin, xanthopterin and erythropterin—not direct derivatives of uric acid, though not without points of community in structure as well as in general physical characters. And the last paper by Hopkins to be published in his lifetime was another communication to the Royal Society in 1942, in which, in his eighty-second year, he returns to the Pierid pigments and brings the latest evidence concerning them, and their pterin structure, into relation with some of his own observations, made and published more than half a century earlier. The former lepidoporphyrin is now renamed 'rhodopterin', and the relation to it of the red substance obtained under like conditions from a uric acid product, no longer to be regarded as one of identity, is left as an unsolved problem, in which Hopkins still sees possibilities of great interest; and Hopkins's instinct in such matters did not usually err. Further, the origin of the pterins and their relation to purine bases and uric acid, which are to be found with them in the butterfly's wings, is the kind of problem which might have commended itself to Hopkins's interest, especially in view of the more recent evidence of the physiological importance of folic acid.

Later Activities at Guy's Hospital

Altogether, including his five years with Stevenson, Hopkins remained at Guy's Hospital more than fifteen years. Probably because his time was divided between clinical study and research, he was rather long in reaching medical qualification, obtaining the Conjoint Board Diploma and the London M.B., both in 1894, when he was thirty-three years old. He had made valuable friends, both among his seniors, such as Hale White and Cooper Perry, and among men more of his own age but senior in standing, such as Wooldridge and Washbourne; but both of these latter had died tragically early, some years before he qualified. With Washbourne, a bacteriologist of great promise early cut short, he had spent Christmas in 1890 with the Hale Whites at Arosa, and on the journey home had visited the Pasteur Institute, seeing Pasteur himself and making fuller contacts with Roux and Bordet. As soon as he qualified he was given an appointment on the school staff, and came under the vigorous and friendly stimulus of work with Starling, recently appointed Lecturer on Physiology. In that department he also met Bayliss and Leathes. Another friendship, which was to last for the rest of their joint lives, was made outside the Guy's circle with A. E. Garrod, with whom he collaborated in important researches on urobilin, and on haematoporphyrin excreted in the urine as the result of certain types of poisoning.

During his last four years at Guy's his time seems to have been much broken

by teaching physiology, mostly, no doubt, on the chemical side, toxicology, and, for a time, elementary physics and chemistry for the preliminary scientific examination. In the last two years he further became involved in an organization for carrying out laboratory tests and examinations, and reporting the results through the post, to medical practitioners requiring them for diagnosis or guidance of treatment. This was to grow into the Clinical Research Association; and for the first two years of its existence, Hopkins was in charge of its chemical side. It began its operations in a room in Denman Street, S.W., near to Guy's Hospital, which he and Wade had rented and fitted as a laboratory for their researches. And with all these calls on his time, which he had to accept in order to make a sufficient income, Hopkins still found opportunity for research, and even contrived to engage private assistants to accelerate its progress. It was in this period that he began for the first time to interest himself in the chemistry of the proteins, publishing observations on their halogen derivatives with H. W. Brook in 1896 and on the crystallization of the albumins of blood serum and egg-white with S. N. Pinkus in 1898. Hofmeister, some years before, had shown that by removing the globulins from such fluids by half-saturation with ammonium sulphate and slowly concentrating the filtrate, the albumins could be induced, rather precariously and on a smallish scale, to yield crystals. Hopkins now showed that a careful adjustment of the acidity of such a solution would cause the albumin to separate as crystals in bulk and enable it to be recrystallized any number of times. Certain ordinary animal proteins could thus, for the first time, be obtained in the form of crystals with ease and in any required quantity; and he found that, with repeated crystallization, the elementary composition of such a protein remained unaltered, so that it could reasonably be regarded as a chemical entity. The completion and full publication of this work was not to come, however, till after he had migrated from Guy's Hospital to Cambridge.

Marriage

That decisive turn in Hopkins's career, indeed, was still just ahead of him. If he remained at Guy's, he could now see prospects which many men would have found attractive enough. His position, as the holder of an assortment of part-time posts, with a margin of time for research, was, in those days, that of many men who were waiting for the chance to fill a vacancy on the clinical staff of a hospital. It is probable that such an opportunity would have come eventually to Hopkins, if he had been sure that he desired it and had been willing to wait; and it may even be surmized that, with his unusual scientific equipment, his keenness in penetrating to the heart of a problem and his sympathetic personality, he might have become a highly successful consultant in certain branches of medical practice. On the other hand, if he desired it, it was possible and even likely that he might eventually succeed Stevenson at the Hospital and the Home Office. And there was soon another factor in the situation, which might have involved not only his own desires and ambitions; in 1898 he married. It was in

1893 that he had met and become engaged to Miss Jessie Anne Stevens, who, being an orphan, had been living with relatives at Carlisle, though her family home had been at Ramsgate. She had entered the Royal Free Hospital in London as a Lady Probationer. Hopkins's uncertain prospects had made the engagement a long one, but by 1898 these seemed to promise sufficient stability to justify them in entering upon a life partnership, which was to be a serenely happy one, marked by a most intimate comradeship and confidence. They began their married life in a flat at the top of a building in Lincoln's Inn Fields. In the flat on the floor below them a young Scotsman, who was beginning to make his way as a political organizer and journalist, J. Ramsay MacDonald, was living with his wife. Mrs MacDonald's family connexion with scientific circles—she was a daughter of Dr J. H. Gladstone, F.R.S.—might eventually have provided a link of interest between the two couples, had Hopkins and his wife lived there for more than a few months. As it was, their only encounter came in circumstances of some agitation. MacDonald, distracted father, appealed to the Hopkins to take charge of his wife, while he fetched the doctor to deal with the unexpectedly early arrival of his first-born; and so, as physician and nurse, they presided over the birth, which was completed before the doctor came. The acquaintance went no further, because Hopkins moved soon afterwards from London; and it was not renewed until, nearly thirty-five years later, presiding at the Anniversary Dinner of the Royal Society, he greeted the Prime Minister, Mr Ramsay MacDonald, as one of the principal speakers.

Cambridge

The turning point, which was to mean so much for biochemistry as well as for Hopkins, came at a meeting of the Physiological Society at Cambridge, in May 1898. As Hopkins came out of Christ's College, where the Society had dined after its laboratory meeting, Michael Foster overtook him and, with a friendly hand on his arm, invited him there and then to come to Cambridge, in order to develop teaching and research on the chemical side of physiology. Foster, though his earlier comprehensive interest in physiology was by that time in competition with parliamentary and other public activities, still had a remarkable faculty for keeping in touch with promising new developments; and there is reason to believe that Starling, who had enjoyed opportunities for judging Hopkins and his work at close quarters, had brought both to Foster's notice. In any case, here was an opportunity of doing something effective for scientific development, along the lines on which Hopkins himself had already given evidence of distinguished ability, and promise of even much greater achievement. In spite of his claim, perhaps only half serious, that the collecting of the vapour ejected by the bombardier beetle had made him, already in 1878, a biochemist at heart, it must be remembered that even twenty years later, when Foster invited him to Cambridge, biochemistry, as a recognized branch of scientific study, existed nowhere in the world under that name and in Britain hardly at all. Since its early beginnings with Liebig and Wöhler,

organic chemistry had wandered far from its original objective of the natural products of vital activities of animals and plants; so that its later followers were giving a predominant and still increasing share of their attention to the production by synthesis, first of substances analogous to certain of the natural products, largely those of vegetable origin, and then of other carbon compounds, increasingly remote in type from any to be found in nature. Eventually one section of organic chemistry, immensely reinforced in knowledge of methods and synthetic possibilities, was to return to its original aim, and thus to form fresh links with the biochemistry which had grown meanwhile to fill the gap; but that was to be a later development, at the hands of men of whom some were Hopkins's contemporaries, but more his juniors. At the time when Foster made his proposal, the chemistry of natural organic substances and of vital processes had fallen low in achievement, and also in reputation with the official leaders of chemistry, especially in this country. On the continent of Europe this chemistry of living organisms, and especially that of animals, had achieved, though not without opposition, a certain measure of independence. Hoppe-Seyler had founded as early as 1877 his *Zeitschrift für physiologische Chemie*, and the work of such investigators as Hoppe-Seyler himself, Hofmeister, Hammarsten, Salkowski, Duclaux, Drechsel and Kossel stood high in the world's esteem. There had been little development of the same kind, however, in Britain; the earlier researches of one immigrant of genius, J. L. W. Thudichum, had, for one reason or another, been unjustly discredited in his lifetime. At Cambridge especially, what was then termed 'chemical physiology' had fallen on evil days. The one of Foster's pupils who had given promise of successful enterprise in that direction, Sheridan Lea, had fallen out through illness, and the gap had been inadequately bridged, for a year or two, by the efforts of a recent graduate, whose special equipment went little beyond access to Lea's notes for his lectures and practical classes. What Foster, planning for something beyond the range even of his wide vision, offered to Hopkins was, in effect, the opportunity to initiate a creative centre for a branch of scientific knowledge and discipline new to Britain. And, to the lasting benefit of science in this country and far beyond it, in spite of the brightening prospect of a pleasant and dignified career in London, Hopkins decided to go to Cambridge; and, as an important factor in that decision, we must recognize the influence of a wife who could be trusted always to favour any step which would give Hopkins free scope for the development of his special scientific genius.

Emmanuel College

If Hopkins expected, however, that the Cambridge appointment would free him from all hindrances to concentration on his own special interests in science, such hopes were doomed to early disappointment. The lectureship only gave him £200 a year, which even in those days, with no College Fellowship behind it, afforded meagre support for a married man. It was to be substantially supplemented, indeed, by supervisory work with medical students which Emmanuel

College offered; but Hopkins found that the supervision was to cover anatomy as well as physiology and, over-conscientious as always, found it necessary to inflict hours of preparation upon himself and to burn the midnight oil, in order to meet this requirement to his own satisfaction. He continued to do this work, however, and to combine it later with an even heavier load of general responsibilities as Fellow and Science Tutor of Emmanuel College, for twelve years in all. With the preparation needed to enable him, with no previous experience of the kind, to lecture to the advanced (Tripos Part II) class on his own subject, he might well have been thought to have enough of formal obligations to fill all his time; and yet he contrived, even in this period, to find time for researches as brilliant and effective as any in his career.

Tryptophane

Not long after he had begun his teaching for the University, an opportunity for a completely new line of research was presented by an accidental observation in his advanced practical class. The students were performing, as a class exercise, the colour test given by most proteins and known as the reaction of Adamkiewicz, in which, when acetic acid had been added to the protein solution, the subsequent addition of strong sulphuric acid produced a blue colour. One of the students in that first of Hopkins's Cambridge classes—it was the late John Mellanby, F.R.S., Professor of Physiology at Oxford at the time of his death—completely failed to obtain the reaction; and Hopkins himself soon verified the fact that, with acetic acid from the bottle on that particular shelf, it was unobtainable, though readily produced by that from any of the others. I was myself a post-graduate research student at the time, and I well remember meeting Hopkins in the passage as he came from the class laboratory, eager to pass on the news of the puzzling anomaly which he had just encountered. Already he seemed to have recognized its potential importance, and spoke of the possibility that the colour reaction was due to some common and unrecognized contaminant of acetic acid. 'And', he added, with that upward jerk of his shoulders, jig on his feet and whimsical grimace, with which he so often signalled a reaction of excitement to something new or puzzling, 'I have a feeling, Dale, that, if we can find the meaning of a colour-reaction like that, it may open up a way to new knowledge of the structure of the old protein molecule itself'. With the assistance of another member of that class, S. W. Cole, he immediately began the search which led to the recognition of glyoxylic acid as the common contaminant of acetic acid which produced the Adamkiewicz reaction. And then, provided with a much more effective and uniform reagent, they began the search for the other party to the reaction—the chromogenic constituent of most proteins. The course of the successful quest showed, at two points at least, Hopkins's characteristic *flair* for identities and methods. He seemed to regard it almost as self-evident that the substance for which they were looking would be a particular, unidentified constituent of the products of protein hydrolysis, and especially of tryptic digestion, long familiar as the

cause of a rose-red colour reaction to chlorine water or bromine, known as the 'tryptophane' reaction; and by the same kind of incommunicable instinct he seemed to know that a 10 per cent solution of mercuric sulphate in 5 per cent sulphuric acid would be worth trial as a specific precipitant for this substance. So tryptophane was isolated, the main features of its constitution were determined and its structure was, in effect, identified; although, of the two isomeric possibilities, they thought that it was probably skatol-glycine, whereas Ellinger proved some years later, by synthesis, that it was the alternative, indol-alanine.

Qualitative Nutrition Studies

This isolation and identification of tryptophane, as a new and most significant amino-acid constituent of most proteins, was in itself an achievement, but for Hopkins it was to provide also the opening of a new chapter of his researches. The identification of the other amino-acid 'bricks' of the protein architecture had meanwhile been proceeding apace at the hands of Emil Fischer, Kossel and others, and Hopkins was thus soon in a position to test the importance, in the protein part of a dietary, of the presence of each of these constituents of the complete protein molecule, and of tryptophane in particular. Hitherto the conception of an adequate diet had been in terms of proteins, fats and carbohydrates, and, so long as the requirements of nitrogen and sulphur for the replacement of wear and tear were met, had paid little attention to anything but crude energy values, though it had long been known that gelatin, through an aromatic deficiency of its constitution, could not wholly replace natural proteins. The conception of a *qualitative* adequacy of the protein part of a diet, however, was first brought clearly into view and given a precise meaning by the publication in 1906 of an investigation by Hopkins and Miss Willcock, in which they showed that a diet in which zein (from maize) was the sole protein constituent, however great its amount, was inadequate to maintain weight and growth in young rats, and that the addition of tryptophane to such a diet would produce an important though not an indefinite prolongation of life. They concluded that the continued inadequacy was probably due to lack of lysine, which, like tryptophane, was known to be absent from the zein molecule. Ten years later, in 1916, Hopkins was to prove, with Ackroyd, that a diet must contain either arginine or histidine, but that either of these diamino-acids could replace the other.

Accessory Food Factors (Vitamins)

Even in 1906, however, Hopkins had already advanced in conviction far beyond the necessity of certain amino-acids in the protein component of a diet, as the only factor determining its qualitative adequacy. In an address which he gave to the Society of Public Analysts in that year he made this definite and, at that time, highly significant statement:

> 'No animal can live upon a mixture of pure protein, fat and carbohydrate, and even when the necessary inorganic material is carefully supplied the animal still cannot flourish.'

There, of course, is in essence the recognition of the accessory factors, required in a diet already adequate as a source of energy, and later to be known as 'vitamins'. Subsequently it came to light that there existed publications, long effectively forgotten, in which Lunin in 1888 and Socin in 1891, both working in Bunge's laboratory, had obtained evidence in favour of such a conclusion; while in 1905, the year before Hopkins's statement quoted above, Pekelharing had published, in a form which had failed to bring it to general notice, the statement that milk contains a substance which, even in very small amounts, has an extremely important effect on the nutritional value of a diet, and had thereby anticipated the central thesis of Hopkins's important paper of 1912. This latter must be regarded as his main experimental contribution to the vitamin story. It provided a stimulus and the essential features of a method for a large part of the world-wide outburst of investigations in this field, which soon came in a flood. When he later discovered the extent to which his main conclusion had been anticipated, Hopkins was anxious to do justice to the earlier discoverers and to consider, as in his Nobel lecture in 1929, the reasons for the general oblivion which had overtaken their publications. There could be no doubt, however, that his own experiments represented a fresh and independent attack on the problem; and they had been planned with such a care for uniformity of all conditions except the one under test, and carried out with such quantitative detail and in a manner so strictly comparative, that the results not only gave convincing evidence of the need for the unidentified 'accessory factors' in the diet, but established the fact that they performed an essential function in the metabolism of normal maintenance and growth, and were not merely promoters of appetite. To complete the story, however, it ought to be mentioned that, convincing and stimulating as these experiments were at the time of their publication, nobody afterwards, not even Hopkins himself, was ever able to obtain the same result again, under conditions which seemed to be identical in every recorded detail. The small ration of milk which he gave did not, in fact, contain enough of the vitamins, in particular not enough of the B-vitamins, to make adequate an otherwise vitamin-free diet. Many years afterwards he came to the conclusion that these pioneer observations must have involved the phenomenon which Fredericia had later described as 'refection'—an accumulation of starch in the caecum, providing the physical basis of a pabulum for the growth of bacteria which synthesize B-vitamins. This did not mean, of course, that Hopkins's general conclusion had been wrong, but merely that the evidence on which he had based it had been complicated by a factor which was not only unknown, but was not even discoverable in the light of what was known of such matters for many years after 1912.

Hopkins's popular reputation as a biochemist was based very largely on this work leading to the recognition of the vitamins. This, further, was the explicit ground of the award to him, in 1929, of the Nobel Prize which he shared with Eijkman, who had discovered in 1890 the connexion between beri-beri and an exclusive diet of decorticated rice. It may well seem anomalous that such fame, endorsed by an international verdict of such high authority, should rest, in the

main, on Hopkins's publication of one paper dealing in detail with his experiments, important and influential as this was. It is not the only instance, in fact, of his influence on the development of a new set of ideas, extending widely beyond the range to be expected from his modestly published record of his own direct, experimental contribution. Concerning the origin of the vitamin story, it was known to many who were in close touch with Hopkins, and through them it had become known to a wider circle, that he had been working on the subject for years before he felt ready to put on record the evidence for his conclusions. We have seen that he had mentioned these briefly to the Analysts as early as 1906; and in 1909, in lectures delivered at Guy's Hospital, but never properly published because of an illness, he had developed them more fully. He had, in fact, been working hard on this problem from 1907 to 1909, though the housing and equipment then available at Cambridge for his experiments were almost incredibly bad. From private notes which he left, it can be stated that in this period he had been the first to use yeast as the source of 'accessory factors'; and, since butter was then the fat-component of the artificial diet given to his rats, he had obtained a ration complete in all essential constituents for this species. He was actually preparing a paper on these experiments in 1910, when he unwarily brought his head into sharp contact with an iron staircase, and the resulting concussion, not of a serious degree in itself, initiated, or perhaps only precipitated, the onset of a severe neurasthenia. Long-continued overwork was certainly another important factor, and the illness kept him out of effective research for most of a year. When he returned to his nutritional experiments in 1911, he had obtained an alcoholic extract from some hundredweights of yeast, made for him commercially; but, having now substituted lard for butter in the artificial diet-mixture, he had produced another deficiency, of a kind then unknown, so that the yeast extract no longer sufficed. It is known also that he had postponed publication of his earlier results, in the hope that he might be able to produce evidence concerning the chemical nature of the yeast factors. What he published in 1912, dealing chiefly with the effect of small additions of fresh milk, was regarded by him, at the time, as a side issue from the main work in which he had been using yeast, and of which the results were never to be published at all. It soon became clear that many other workers were entering this field, most of them with immeasurably better facilities than those with which Hopkins had come so near to making an advance, in detailed discovery, far beyond any which he was in a position to claim. There could be no doubt, in any case, of the general approbation which greeted the award of a Nobel Prize, recognizing the leading part which he had played in opening to investigation a field so rapidly extending, and so fruitful in further possibilities, as that of the 'vitamins'. It may perhaps be permissible to express regret that he did not make early use of the right, which would have been generally accorded to him, to prevent the general application, to this chemically heterogeneous group of substances, of a name so obviously inappropriate to many of them.

Intermediary Metabolism

In his own private judgment Hopkins never gave the highest rank, among his various research enterprises, to this pioneer work on the vitamins; and he was the more ready to leave its further development to other hands, in that his chief interest had already found a stronger attraction in what, at least in retrospect, he regarded as the true and central aim of the whole of his life of research, for which all his earlier work had only prepared the way. This was an experimental attempt to unravel the tangled skein of 'intermediary metabolism'—the complex of linked chemical reactions, mainly oxidations and reductions, catalyzed by a series of intracellular enzymes, having 'tissue respiration' as its end result and the provision of energy for the mechanism of life as an all-important function. When Hopkins began his work, the prevalent tendency was still to regard such processes as beyond the reach of investigation. In an address given in 1935 Hopkins quoted a statement made at a much earlier date by his friend and patron, Michael Foster, that

> ' . . . we cannot yet trace the steps taken by the oxygen from the moment it slips from the blood into the muscle substance to the moment when it issues united with the carbon as carbonic acid.'

On which he commented that:—

> 'Insofar, however, as the progress of metabolism . . . was ascribed in concrete thought to hypothetical qualities emergent from a protoplasmic complex in its integrity, or when substances were held to suffer change only because in each living cell they are first built up, with loss of their own molecular structure and identity, into this complex, which is itself the inscrutable seat of cyclic change, then serious obscurantism was involved.'

When he entered the field he had found the position thus dominated by the conception of the 'biogen', a giant molecule within which inscrutable chemical changes took place; and it was his mission to slay that giant. During the years following 1912, indeed, he repeatedly took opportunities, presented by addresses to wider audiences, to develop this theme of the duty and the practicability of dissecting these processes of intermediary metabolism into recognizable reactions of ordinary chemistry, taking place with great speed under the influence of enzymes spread on intracellular surfaces; and on such occasions he would review, at intervals, the excitingly rapid progress of knowledge in this field. These addresses still retain their stimulating quality; they give an invaluable record of the movement and development of Hopkins's thoughts in those years, and of the way in which the general body of ideas was being continuously refreshed and refashioned, by the impressive sequence of discoveries, among which those of his own co-workers and pupils were playing a notable part. Among these reviews and professions of faith, before various audiences, all of which abundantly repay study, special mention may be made of the addresses

to the Section of Physiology of the British Association as its President at Birmingham, in 1913, and to the whole Association as its President at Leicester, in 1933; the Herter Lectures at Baltimore in 1921; and the Inaugural Lecture to the International Physiological Congress at Stockholm, in 1926. And this central interest of Hopkins's later years, this point towards which he regarded the whole of his scientific life as having grown, was appropriately recognized when a number of investigators, all of whom had had the privilege of working in his laboratory and feeling the inspiration of his thought, celebrated his seventy-fifth birthday by publishing in the following year, 1937, a collection of articles dealing with 'Perspectives in Biochemistry'. The first of these articles, by his colleague, J. B. S. Haldane, opened with the claim that 'The ultimate aim of biochemistry may be stated as a complete account of intermediary metabolism'.

Muscle and Lactic Acid

The first direct contribution made by Hopkins to the quantitative study of a constituent process of this intermediary metabolism, and one of the earliest from any source, may be found in the part which he took in joint work with his friend, Walter Fletcher, on the metabolic changes accompanying contraction, recovery and *rigor mortis* in surviving frog's muscle. Precise methods of analysis were applied, for which Hopkins was responsible, and he took the opportunity to describe a new colour reaction for lactic acid which he had introduced two years earlier for use in his class. To both authors was due the special merit of revealing the fallacies inherent in earlier attempts of this kind, through the formation of lactic acid during grinding and extraction of the muscle, and of excluding these by carrying out the disintegration in ice-cold alcohol. For the first time, probably, they had been able to arrest such a metabolic process in a living tissue at chosen stages, and to submit the resulting extracts separately to quantitative determinations. The work had again a pioneering character, and laid the foundation for the series of further researches by A. V. Hill, O. Meyerhof and many others, which established on a firm basis the metabolic cycle of carbohydrate, and the liberation of energy thereby for the contractile function of muscle. For many years the appearance of lactic acid at a stage in this cycle was held also to determine, in some way, the change of tension in the muscle fibre; and a full presentation of this view was given by Fletcher and Hopkins in their joint Croonian lecture to the Royal Society in 1915. As is well known, the attribution of this function to lactic acid was, after some years, overtaken and eliminated by more modern discoveries of the complex cycle of changes affecting the phosphorylated bases in muscle, and the relation of these to the muscle-protein myosin. The research of Fletcher and Hopkins, however, still retains intrinsic value, in addition to its historic importance, as the introductory passage of one of the great chapters of modern biochemistry. It vindicated the claim that metabolism, as a dynamic process, was accessible to study in detail by methods of exact chemistry.

Changes of Status and Opportunity at Cambridge

The other main items of the personal researches, by which Hopkins contributed to the study of intermediary metabolism, were carried out under very different conditions from those under which he had been working, in Cambridge, up to the sudden beginning of his illness in 1910. It will be convenient, therefore, to sketch briefly at this point the changes in his position and in the facilities available to him during the rest of his career. He went to Cambridge, as we have seen, as a University Lecturer in 1898; in 1902 his appointment was raised to the status of a Readership, Emmanuel College contributing to the stipend and, four years later again, in 1906, making him Science Tutor to the College. These appointments together gave him a sufficient income to support his family, but the multiple demands on his time and mental energy had at least prepared the way for the illness which ensued. This threat of disaster, however, brought its own relief, in the news that Trinity College, recalling, no doubt, its initiative many years earlier in bringing Michael Foster to Cambridge, had decided in 1910 to offer Hopkins an appointment as Fellow of the College and Praelector in Biochemistry—a post which, added to his Readership, provided him with sufficient income, but involved practically no duties beyond the continued development of his own ideas in research. He accepted joyfully, and Emmanuel College elected him to its honorary Fellowship on his transfer to Trinity. In notes which he left behind him, Hopkins more than once expressed the hope that, in any obituary notice which might be written of him, prominence would be given to the debt of gratitude which he owed, to Emmanuel College for its support in his earlier Cambridge years, but especially to Trinity College, for its provision of the way of escape from what was becoming an impossible burden, and to his devoted friend Walter Fletcher, whose advocacy he believed, no doubt rightly, to have been effective in moving the College to its far-sighted and generous decision.

Thus, on recovery, he returned to greatly improved conditions for research, so far as time and freedom for study and thought were concerned. His accommodation for such work, however, was still almost incredibly bad according to the standards of to-day. His chemical work had all been done in one small and ill-found laboratory room in the department of physiology, and with the minimum of assistance even in a menial capacity; while for his experimental rats, needing quite special care and attention, the only available accommodation was in a cellar. And these conditions remained unchanged until 1914, when Hopkins's university appointment was raised to the status of a separate Chair of Biochemistry, and, with the removal of Physiology to the new Institute which had been built for it, the Department of Biochemistry secured the reversion of a greatly extended share of the old building.

The First World War followed, of course, soon after this change had been effected. Hopkins found research difficult while it lasted, and students of all stages were few. He became an effective member of the Royal Society's war-time Food Committee, and managed to carry out investigations for it; but, like

others who were well past middle age at that time, he hankered after fuller employment on national duty. His wife, on the other hand, found abundant outlet for her nursing experience and organizing ability in the temporary military hospital established in Cambridge; and the recognition of her services by the award of the R.R.C. gave him great pride and satisfaction.

When the war ended the new department was soon well under way, and biochemistry achieved recognition as a separate subject for Part II of the Natural Sciences Tripos. Soon the accommodation in the old physiological department became inadequate for the many who wished to do research under Hopkins's guidance, and a grant from the trustees of the Beit Memorial Fund for Medical Research enabled him to rent a disused laboratory, known as the Balfour Laboratory, where students of Newnham and Girton Colleges had formerly had their practical classes, before women were admitted to the University laboratories; and there most of the further biochemical researches were carried out until 1925. In 1923–1924, the trustees of the estate bequeathed by Sir William Dunn, again in response to Walter Fletcher's recommendation, decided to make a large grant to Cambridge University for the endowment of a special Chair and the provision of a handsome Institute for Biochemistry. The new Institute was opened by Earl Balfour, then Chairman of the Medical Research Council as well as Chancellor of the University, in 1925, and for the remainder of his tenure Hopkins and his department, with a brilliant succession of distinguished visiting workers, enjoyed the occupation of a building which had planning and dignity as well as effective equipment. Hopkins became the first Sir William Dunn Professor, and J. B. S. Haldane the first Reader, with a special responsibility for the research workers. This division of function suited Hopkins well; for while, like all men with the research instinct, he resented on occasion the broken time which teaching involves, he enjoyed the contact with fresh and eager young minds. On the other hand, while he was always, perhaps for his own sake even too readily, available for discussion with anyone engaged in research in his department, he never exercised authority or imposed suggestions concerning the choice of problems or the detailed conduct of a research. He himself worked as often alone as in collaboration, and, towards the end, as a rule with only his faithful technician and co-worker for many years, James Morgan. When I once commented to him on the success of a friend of both of us, in doing research in the isolation of a private laboratory, and expressed doubt whether I myself could work effectively under such conditions, he rather surprised me by the unhesitating conviction of his reply. 'Oh! I am sure that I could'. And I believe that, in fact, he found the conditions most favourable to his research, and most congenial to his temperament when thus engaged, in a comparative privacy, in which he could think his own thoughts and use his own hands and eyes, while they lasted, in personal experiments and observations at every stage and on every detail of a research. He had none, I think, of the managerial instinct, which has enabled some famous scientists to do research by assembling and interpreting the results of experiments which others have carried out at their behest. On the other hand, he had great enjoyment and

profit, giving and gaining much, from the daily chances of contact and exchange of experience with such a wider circle of brilliant and enthusiastic investigators as his own Institute provided. It was a cheerful and friendly, as well as an able and stimulating community, of which he naturally became the central and almost legendary figure—the great little chief, great in inspiration and in scientific wisdom as he was small and slender in physique. He was their incomparable 'Hoppy'—an inevitable and wholly affectionate diminutive, with no hint of disrespect in its habitual use. He basked in the glow of the admiring comradeship with which they surrounded him.

Glutathione, Xanthinoxydase and other Researches

Both of Hopkins's own major direct contributions to the elucidation of intermediary metabolism, or tissue respiration, were begun while his department was still housed in the old physiological and Balfour laboratories, though their continuation, and most of the great developments in that field for which his pupils and colleagues were responsible, took place after the removal to the new Dunn Institute.

The first was the isolation by Hopkins in 1921 of a substance which contained an SH group, readily and reversibly oxidizable to an S—S linkage, and which was found to be widely distributed, especially in rapidly multiplying cells of both plants and animals. For some years, following his own precepts, he had been engaged in the attempt to identify, no matter how small the quantities, products of metabolic change caught, as it were, during their fleeting appearance in a chain of reactions. He had been applying the nitro-prusside colour reaction, as modified by his pupil Rothera for the detection of excretory products in ketosis, such as aceto-acetic acid. It led him, however, to a substance already known by a reaction as 'philothion', as formerly he had tracked the substance known by a different reaction as 'tryptophane'. The presence of something in living cells characterized by a thiol group and reacting thus with nitroprusside had been recorded by Heffter and others. This Hopkins now succeeded in isolating and identifying and, believing it to be a dipeptide of glutamic acid and cystein—it seemed to be glutamyl-cystein according to experiments by a group of his pupils—he named it 'glutathione'. In 1927 experiments by Hunter and Eagles made it clear that the constitution was less simple than this, and Hopkins, returning to the problem, isolated sufficient of the substance to enable him to purify it completely and examine it more fully, with the result that in a second paper, in 1929, he proved that it was a tripeptide of glutamic acid, glycine and cystein. For this second investigation he isolated glutathione by one of those elegant devices, at which he seemed to arrive without any process of reasoning which he could make clear; it formed a beautifully crystalline cuprous salt, but little soluble in water, in which form it could readily be isolated by precipitation. The function of this autoxidizable peptide as a carrier of oxygen, or acceptor of hydrogen, was then to form an important chapter in the researches of his pupils and associates on processes of tissue respiration.

The other major direct contribution to the progress of knowledge in this field, to which Hopkins's own name is attached in the published record, was the discovery of a specific enzyme, widely distributed in the tissues and readily accessible for isolated study in milk, which catalyses oxidation of the purine bases, xanthine and hypoxanthine, to uric acid. So his earliest biochemical interest made contact with the later and predominant one. The paper, published by Morgan, Stewart and Hopkins in the Royal Society's *Proceedings* in 1922, has become one of the classics of the subject. Hopkins had found, in the course of his separation of glutathione, that there was something in a mixed precipitate of bases which caused the reduction of methylene blue when added to milk; but it was his constant assistant, E. J. Morgan, who first found that the base in question was hypoxanthine, and whose name, accordingly, stood first in the title of the paper.

These two discoveries of glutathione and the xanthine oxidase, not only by themselves provided starting-points for a large number of important researches by Hopkins's immediate pupils and associates; they helped also to create a stimulating atmosphere of interest in the wider field of investigation, dealing with intermediary metabolic processes in general. Mention may, perhaps, be made of one series only, for which work in the Dunn Institute had a particular responsibility, in the studies of enzymatic processes in suspensions of 'resting' bacteria, originating with Marjory Stephenson and J. H. Quastel and continued by a succession of Dr Stephenson's later co-workers. To attempt any kind of survey, however, of the important and widely ranging lines of research which were followed by workers in the Institute, under Hopkins's inspiring but easily tolerant and unexacting leadership, would lead far beyond the limits of such a notice as this. Those concerned have carried far and wide, to other centres of enterprise in biochemical research, the great tradition which grew under Hopkins's influence. And it is pleasant to think of the eager interest with which, in his later years, he must have watched the convergence of lines of research which his own work had done so much to initiate, as one after another of the vitamins came to be recognized as a participant, as co-enzyme or substrate, in some essential reaction of intermediary metabolism.

His own direct participation in research was interrupted, between the ends of the years 1930 and 1935, by his duties as President of the Royal Society; and, when those came to an end, he had but a few years of freedom before health and then eyesight began to fail. Nevertheless, as we have seen, the new evidence as to the nature of his butterfly pigments stimulated him to take up the subject again. Later again, and always with Morgan's increasingly close and indispensable collaboration, he took up once more the problem of the part of glutathione in intermediary metabolism, now as the specific co-enzyme of glyoxalase, both enzyme and co-enzyme being found in almost all plant and animal tissues. He left the significance of this wide distribution as a problem still to be solved; but, when he died, a further paper on glyoxalase with Morgan was already in the press. And, as a side-issue, perhaps, of the work on xanthine oxidase, he had earlier published, in 1944, the results of experiments carried

out with Mrs Simon-Reuss, showing a remarkable stimulating effect on the growth of tissue-cultures, produced by adding a small proportion of hypoxanthine to the nutrient medium.

Official Duties and Honours

Hopkins found an opportunity for influence on the public recognition of research in the field of medicine, and of biochemistry in particular, when in 1913 he became a member of the first Medical Research Committee, administering the first annual grant of public money to be made for the support of researches in a wide field, which had been established under the National Health Insurance Act. He was thus responsible for the recognition of biochemistry as one of the main divisions of research activity for which provision was to be made in the then projected National Institute for Medical Research; and I may be allowed in gratitude to recall, incidentally, that my own eventual appointment to the first scientific staff of that Institute was entirely due to Hopkins's insistent recommendation. He had no particular gifts of forcefulness, or adroitness, as a Committee-man; but on that Committee, as in many other connexions, he obtained a position of strong influence by his transparent sincerity and by the quiet but unwearying persistence with which he advocated a policy in which he believed. In the Medical Research Committee and its successor, the Medical Research Council, he always retained a keen interest and something of a founder's pride; and it was through Hopkins that the name of Walter Fletcher, the friend to whom his own career had owed, and was still to owe so much, was put forward for consideration as its first Secretary—an appointment which was to be of such historic importance for all the interests of medical research in this country, including the manner of its support from public funds. When Fletcher died, he was succeeded in that post by a devoted pupil of Hopkins, Edward Mellanby.

All kinds of recognition soon began to come to Hopkins, from the list of which only a selection can here be mentioned. In 1918 he received a Royal Medal from the Royal Society, and in 1925 the public honour of a knighthood; *Brighter Biochemistry*, the sprightly journal of his department, was bound, of course, to devise a coat of arms for him, with the motto 'Gluta thy Owne'. In the following year he received the Royal Society's Copley Medal, and four years later again, in 1930, what he certainly regarded as the crowning recognition of the place which he and his work had won in the esteem of the scientific world, in his election to be President of the Royal Society. His tenure of the Chair, from 1930–1935, fell in one of the most normal periods for science, between the subsidence of one war's disturbance and the gathering threat of another. He carried out the duties of the office, as of all others, conscientiously and with quiet dignity. He had not the voice for oratory, and never learned the effective use of a microphone; but his speeches and addresses were full of stimulating thought and cast in attractive literary form. Like the public utterances of some of his predecessors in that Chair, they might present a problem to those who claim that an effective use of English is only to be attained by

those who have received an intensive education in the classics. As illustrating the breadth of his scientific vision, and his power of presenting with a vivid accuracy the essential features of recent developments in a wide range of scientific activities, his Presidential address in 1933 may be cited as specially worthy of study. His position as President of the Royal Society led, indeed, to his being asked to accept responsibilities which were unlikely otherwise to have come to him; for example, in 1934, at the special request of Mr Ramsay MacDonald, then Prime Minister, he became Chairman of a Committee on Cattle Diseases under the Economic Advisory Council. In 1935, the last year of his Presidential term, he was awarded the Order of Merit. On 9 October 1937 there was the pleasant occasion, already mentioned, on which a gathering of Hopkins's pupils, with a few older friends who had never been pupils in a formal sense, held a delayed celebration of his seventy-fifth birthday and presented the commemorative volume of *Perspectives in Biochemistry*, at a dinner in Emmanuel College.

Hopkins was a man of small physique, with slender bones, very light musculature and not an ounce of superfluous flesh; but the slight frame was crowned by a finely modelled head, with a brow of noble proportions. His face, with a droop of moustache, had habitually a pondering expression, but the mobile features were easily lit by eager attention, relishing humour, or by the sympathy which made him so ready to share the troubles of others. His friends were apt to think, on occasion, that he was even too generous in spending time and emotion thus, on behalf of some who had no adequate claim on them; but none who knew him well could have failed to experience a quality in his friendship, which made the mere description of doubts and difficulties to Hopkins seem to bring a solution within easier reach.

Though Hopkins was physically so slight and looked rather frail, and though he had no apparent liking for any kind of muscular activity, taking the minimum of bodily exercise involved in a daily gentle walk from his house, through the 'backs' of the Colleges, to his laboratory and home again, he had, till near the end, a quite remarkable equability of health. The nervous disturbance, following an accidental concussion, has been mentioned; apart from that, until he was seventy-seven years old, in 1938, he seemed to have escaped illness of any kind. I remember his telling me that until he had entered the fifties in age he could not remember having had experience even of a common cold. In 1938, however, he had to undergo an operation which, though not serious in itself, left an infection from which he was never to be thoroughly freed, and which caused an increasing unease for the rest of his life. Then came slight, unpredictable attacks of a localized paralysis, an increasing arthritis in a hip and, most difficult of all to bear, an impairment of vision so serious that, though he could just find his way about, he became dependent entirely on others for reading and for manipulations at the laboratory bench, which, till near the very end, he could not make up his mind to desert. And, as we have seen, his fidelity was justified by a continued output of work of interest.

In his last years Hopkins's thoughts were centred increasingly on the cause

for which he had worked so long, so earnestly and with such success—the establishment of biochemistry as a separate scientific discipline, on a footing of equality with others. Fear lest the position which he had won for it at Cambridge might not be fully maintained after him, made him hesitate to take the retirement which he had so abundantly earned. He had, indeed, lived through and played a leading part in the formative epoch of its history; and he died at last with an assured conviction that the cause had passed into safe hands. He is survived by Lady Hopkins, to whose devoted and unintrusive care for him science and the world are deeply in debt; also by two daughters and one son, Mrs Barbara Holmes, who has followed her father into biochemistry and neighbouring paths of research, Dr Frederick Edward Gowland Hopkins, engaged in family medical practice in the country and Mrs Jacquetta Hawkes, sharing archaeological activities with her husband, Professor Christopher Hawkes, and holding a public administrative appointment.

I have been greatly assisted by Lady Hopkins and other members of the family, and am indebted to Dr C. F. A. Pantin for certain details. The fact that Sir Frederick Hopkins himself had fully recorded his memories of the earlier years, and deposited the account with the Royal Society, has alone made it possible to include a number of interesting points of his history. I have further been indebted to Dr Marjory Stephenson's obituary notice in the *Biochemical Journal*, and Sir Edward Mellanby's memorial lecture to the Chemical Society.

H. H. Dale

BIBLIOGRAPHY [1]

1878. Brachinus crepitans. *Entomologist*, **11**, 256.
1889. Note on a yellow pigment in butterflies. *Proc. Chem. Soc.* **5**, 117.
1889–1890. The chemical genesis of physiological pigments. *Guy's Hosp. Gaz.* **3**, 257, 280; **4**, 3.
1890. (With E. H. Starling.) Note on the urine in a case of phosphorus poisoning. *Guy's Hosp. Rep.* **47**, 275.
1891. On the volumetric determination of uric acid in urine. *Guy's Hosp. Rep.* **48**, 299.
1891. Pigment in yellow butterflies. *Nature*, **45**, 197.
1892. On the estimation of uric acid in urine: a new process by means of saturation with ammonium chloride. *Proc. Roy. Soc.* **52**, 93.
1893. On the estimation of uric acid in urine. *J. Path. Bact.* **1**, 451.
1893. Five cases of pernicious anaemia, with determinations of the iron in the viscera, and some observations on the urine. *Guy's Hosp. Rep.* **50**, 351.
1896. The pigments of Pieridae: a contribution to the study of excretory substances which function in ornament. *Phil. Trans. B*, **186**, 661.
1896. (With A. E. Garrod.) Notes on the occurrence of large quantities of haemotoporphyrin in the urine of patients taking sulphonal. *Trans. Path. Soc. Lond.* **47**, 316.
1896. (With A. E. Garrod.) On urobilin. Part I. The unity of urobilin. *J. Physiol.* **20**, 112.

[1] I have tried to make this list of the scientific writings of F. G. Hopkins complete and accurate, and have been greatly helped in the attempt by Miss Ethel Wigmore, Librarian of the National Institute for Medical Research.—H. H. D.

1897. Untersuchung über die Einwirkung der Halogene auf Eiweiss (Vorläufige Mitteilung). *Ber. dtsch. chem. Ges.* **30**, 1860.
1897–1898. (With F. W. Brook.) On halogen derivatives from proteids. *J. Physiol.* **22**, 184.
1897–1898. (With A. E. Garrod.) On urobilin. Part II. The percentage composition of urobilin. *J. Physiol.* **22**, 451.
1898. (With S. N. Pinkus.) Zur Kenntniss der Einwirkung von Halogenen auf Proteine. *Ber. dtsch. chem. Ges.* **31**, 1311.
1898. A modification of Hofmeister's method of crystallizing egg-albumen. *J. Physiol.* **23**, Suppl. p. 47. (*Proc. Fourth Int. Physiol. Congress*, August 1898.)
1898–1899. (With S. N. Pinkus.) Observations on the crystallization of animal proteids. *J. Physiol.* **23**, 130.
1898. The chemistry of urine. *Schäfer's Textbook of Physiology*. Edinburgh and London: Young J. Pentland. Vol. I, 570–638.
1898–1899. (With W. B. Hope.) On the relations of uric acid excretion to diet. *J. Physiol.* **23**, 271.
1898–1899. (With W. B. Hope.) Are nucleo-proteids the chief dietetic precursors of uric acid? a criticism of the conclusion drawn from thymus feeding. *J. Physiol.* **23**, Suppl. p. 46. (*Proc. Fourth Int. Physiol. Congress*, August 1898.)
1899. (With W. Hale White.) On the excretion of phosphorus and nitrogen in leukhaemia. *J. Physiol.* **24**, 42.
1899–1900. On the separation of a pure albumin from egg-white. *J. Physiol.* **25**, 306; *Proc. Camb. Phil. Soc.* **10**, 300.
1901. (With S. W. Cole.) On the proteid reaction of Adamkiewicz, with contributions to the chemistry of glyoxylic acid. *Proc. Roy. Soc.* **68**, 21.
1901. (With S. W. Cole.) A contribution to the chemistry of proteids. Part I. A preliminary study of a hitherto undescribed product of tryptic digestion. *J. Physiol.* **27**, 418.
1902. On the crystallization of albumens. Thesis (MS.) deposited in the University Library, London.
1903. Haemoglobinuric fever: its aetiology. *Dublin J. Med. Sci.* **115**, 410.
1903. (With S. W. Cole.) A contribution to the chemistry of proteids. Part II. The constitution of tryptophane, and the action of bacteria upon it. *J. Physiol.* **29**, 451.
1906. The analyst and the medical man. *Analyst*, **31**, 385.
1906–1907. The utilization of proteids in the animal. *Sci. Progr. Twent. Cent.* **1**, 159.
1906–1907. (With E. G. Willcock.) The importance of individual amino-acids in metabolism. Observations on the effect of adding tryptophane to a dietary in which zein is the sole nitrogenous constituent. *J. Physiol.* **35**, 88.
1907. (With W. M. Fletcher.) Lactic acid in amphibian muscle. *J. Physiol.* **35**, 247.
1907. Vorschläge zur Nomenklatur der Proteine. *VIIth Intern. Physiol. Congr.* (*Heidelberg*).
1907. Four lectures on the significance of variations in the constituents of the urine. *Guy's Hosp. Gaz.* **21**, 327, 382, 403, 423.
1908. Sir Thomas Stevenson. (Obituary notice.) *Analyst*, **33**, 385.
1911. (With H. Savory.) A study of Bence Jones protein, and of the metabolism in three cases of Bence Jones proteinuria. *J. Physiol.* **42**, 189.
1911. Addendum to a paper by F. H. A. Marshall: a note on the chemistry of the vesicular fluid of the hedgehog. *J. Physiol.* **43**, 259.
1912. Feeding experiments illustrating the importance of accessory factors in normal dietaries. *J. Physiol.* **44**, 425.
1912–1913. Dr Pavy and diabetes. *Sci. Progr. Twent. Cent.* **7**, 13.
1913. The dynamic side of biochemistry. Address of Sectional President to Physiological Section, British Association Birmingham Meeting, 1913. *Rep. Brit. Assoc.* 652; also in *Brit. Med. J.* **2**, 713; *Lancet*, **2**, 851.

1913. (With A. NEVILLE.) A note concerning the influence of diets upon growth. *Biochem. J.* **7,** 97.
1913. Acidosis. *Albany Med. Ann.* **34,** 701.
1913. Progress in physiological chemistry. *Ann. Rep. Progr. Chem.* **10,** 190.
1914. Progress in physiological chemistry. *Ann. Rep. Progr. Chem.* **11,** 188.
1915. Progress in physiological chemistry. *Ann. Rep. Progr. Chem.* **12,** 187.
1915. (With G. WINFIELD.) Influence of pancreatic extracts on the production of lactic acid in surviving muscles. *Proc. Physiol. Soc., J. Physiol.* **50,** v.
1915. (With E. M. TRIBE and J. BARCROFT.) Vascular and metabolic conditions in kidneys of rabbits injected with uranium acetate. *J. Physiol.* **50,** xiP.
1916. Newer standpoints in the study of nutrition (a lecture). *J. Chem. Soc.* **109,** 629.
1916. (With H. ACKROYD.) Feeding experiments with deficiencies in the amino acid supply: arginine and histidine as possible precursors of purines. *Biochem. J.* **10,** 551.
1916. Progress in physiological chemistry. *Ann. Rep. Progr. Chem.* **13,** 195.
1916–1917. (With T. B. WOOD.) Food economy in war-time. (Pamphlet.) First ed. 1916; second ed. 1917. Cambridge Univ. Press.
1917. Progress in physiological chemistry. *Ann. Rep. Progr. Chem.* **14,** 171.
1917. (With W. M. FLETCHER.) The respiratory process in muscle and the nature of muscular motion. *Proc. Roy. Soc. B,* **89,** 444 (*Croonian lecture*).
1917. Medicine and experimental science. In *Science and the Nation,* Cambridge Univ. Press, pp. 228–255.
1917. On the choice of food in war-time. *J. State Med.* **25,** 193.
1918. Harold Ackroyd. (Obituary notice.) *Biochem. J.* **12,** 1.
1919. The practical importance of vitamines. *Brit. Med. J.* **1,** 507.
1919. (With H. CHICK.) Accessory factors in food. *Lancet,* **2,** 28.
1919. Medical Research Committee. Report on the present state of knowledge concerning accessory food factors (vitamines). Compiled by a Committee appointed jointly by the Lister Institute and the Medical Research Committee, F. G. Hopkins, Chairman. *Spec. Rep. Ser. Med. Res. Com. Lond.* no. 38, 48 pp.
1919. (With H. CHICK.) Some facts concerning nutrition, for the guidance of those engaged in administration of food relief to famine-stricken districts. (Memo. on 'The Importance of Accessory Factors in Food', by Committee on Accessory Food Factors (M. R. Comm. and Lister Inst.).)
1920. (With OTHERS.) The present position of vitamines in clinical medicine. (A series of papers.) *Brit. Med. J.* **2,** 147.
1920. (With OTHERS.) Treatment and management of diseases due to dietetic deficiences. (A discussion.) *Proc. Roy. Soc. Med.* **13,** Sect. Therap. and Pharmacol. 1.
1920. (With OTHERS.) Acidosis in disease. (A discussion.) *Brit. Med. J.* **2,** 69.
1920. Note on the vitamine content of milk. *Biochem. J.* **14,** 721.
1920. Effects of heat and aeration on the fat-soluble vitamine. *Biochem. J.* **14,** 724.
1920. Balance in nutrition. *Brit. Med. J.* **2,** 862.
1921. Recent advances in science in their relation to practical medicine and the nutritional requirements of the body. (Huxley lecture.) *Lancet,* **1,** 1.
1921. (With C. G. L. WOLF.) Purine metabolism and its relation to gout. Oxford Medicine (Loose Leaf). Ed. H. C. Christian, **4,** 97. Oxford Univ. Press.
1921. An autoxidisable constituent of the cell. *Biochem. J.* **15,** 286.
1921. Some oxidation mechanisms of the cell. *Bull. Johns Hopk. Hosp.* **32,** 321.
1921. The chemical dynamics of muscle. *Bull. Johns Hopk. Hosp.* **32,** 359.
1922. (Chandler Medal Award.) Medal address. Newer aspects of the nutrition problem. New York, Columbia Univ. Press, 1922. *Ind. Eng. Chem.* **14,** 64.
1922. (With M. DIXON.) On glutathione. II. A thermostable oxidation-reduction system. *J. Biol. Chem.* **54,** 527.
1922. (With E. J. MORGAN and C. P. STEWART.) On the anaerobic and aerobic oxidation of xanthin and hypoxanthin by tissues and by milk. *Proc. Roy. Soc. B,* **94,** 109.

1922. (With C. R. W. ADEANE and OTHERS.) Lactalbumin. *Brit. Patent*, 202, 517, 25 August 1922.
1923. V. A. H. H. Onslow. (Obituary notice.) *Biochem. J.* **17**, 1.
1923. An oxidative mechanism in the living cell. *Chem. Ind.* **42**, 676; *Lancet*, **1**, 1251.
1923. Present position of the vitamin problem. *Brit. Med. J.* **2**, 691, 748.
1924–1925. Biochemistry: its present position and outlook. (Huxley Memorial lecture.) *Lancet*, **1**, 1247; *Klin. Wschr.* **4**, 857.
1925. Glutathione. Its influence in the oxidation of fats and proteins. *Biochem. J.* **19**, 787.
1925. (With M. DIXON.) Ueber die Isolierung des Schardingerenzyms aus Milch. Eine Richtigstellung. *Biochem. Z.* **159**, 482.
1925–1926. Criteria of an efficient diet. *Practitioner*, **114**, 7; **116**, 214.
1926. On current views concerning the mechanism of biological oxidation. (With a foreword on the institutional needs of biochemistry.) *Skand. Arch. Physiol.* **49**, 33.
1926. Ueber die Notwendigkeit von Instituten für physiologische Chemie. *Münch. med. Wschr.* **73**, 1586.
1927. The isolation of glutathione. *J. Biol. Chem.* **72**, 185.
1927. (With OTHERS.) Discussion on minutiae of nutrition: do they bear upon practical dietetics? *Trans. Med. Soc. Lond.* **50**, 233.
1928. Accessory Food Factors Committee. Estimation of vitamin A in cod-liver oil. Comparison between the colorimetric (Rosenheim, Drummond) and the biological method. *Lancet*, **1**, 148.
1928. The centenary of Wöhler's synthesis of urea (1828–1928). *Biochem. J.* **22**, 1341.
1928. Das Schwefel-System. *In* Oppenheimer: *Die Fermente und ihre Wirkungen*, **3**, 1144. Leipzig: Vögel.
1929. Crystalline tripeptide from living cells. *Nature*, **124**, 445.
1929. Glutathione: a reinvestigation. *J. Biol. Chem.* **84**, 269.
1930. The earlier history of vitamin research. (Nobel lecture delivered on 19 December 1929.) *Les Prix Nobel en* 1929 (*Stockholm*, 1930).
1930. Denaturation of proteins by urea and related substances. *Nature*, **126**, 328, 383.
1931. (With K. A. C. ELLIOTT.) Relation of glutathione to cell respiration with special reference to hepatic tissue. *Proc. Roy. Soc. B*, **109**, 58.
1931. Problems of specificity in biochemical catalysis. (*Thirty-third Robert Boyle lecture.*) London: Oxford Univ. Press, 20 pp.
1931. Nutrition and human welfare. *Nutr. Abstr. Rev.* **1**, 3.
1931. Possibilities of research on biochemical lines. *Jungfraujoch Sci. Stat.* 1931, p. 70.
1932. Introductory paper, in discussion on recent advances in the study of enzymes and their action. *Proc. Roy. Soc. B*, **111**, 280.
1932. Some aspects of biochemistry. The organising capacities of specific catalysis. (The second Purser Memorial lecture, delivered at Trinity College, Dublin, 14 June 1932.) *Irish J. Med. Sci.* July 1932, p. 333.
1932. Address of the President. Anniversary meeting, 30 November 1931. *Proc. Roy. Soc. A*, **134**, 533; *Proc. Roy. Soc. B*, **109**, 404.
1932. Vitamins as necessities for life. *Broadcast National Lecture.* B.B.C. London, 1932.
1932. Atomic physics and vital activities. (From the anniversary address to the Royal Society, 30 November 1932.) *Nature*, **130**, 869.
1933. Some chemical aspects of life. (Presidential address to British Association, Leicester meeting, 1933.) *Brit. Assoc. Rep.* 1933; also *Chem. Ind.* **52**, 719; Suppl. to *Nature*, **132**, 381; *Science*, **78**, 219.
1933. Chemistry and life. (*Gluckstein Memorial lecture.*) Institute of Chemistry: London.
1933. Address of the President. Anniversary meeting, 30 November 1932. *Proc. Roy. Soc. A*, **139**, 1; *Proc. Roy. Soc. B*, **112**, 159.
1933. Chemical organization in the living cell. *Lancet*, **2**, 573.
1934. Address of the President. Anniversary meeting, 30 November 1933. *Proc. Roy. Soc. A*, **143**, 242; *Proc. Roy. Soc. B*, **114**, 181.

1934. (With F. E. Smith.) William Bate Hardy. (Obituary notice.) *Roy. Soc. Obit. Notices* 3, 327.
1934. William Bate Hardy. (Obituary notice.) *Biochem. J.* **28**, 1149.
1934. Some chemical aspects of life. *Smithsonian Rep.* p. 129.
1934. William Hyde Wollaston Memorial Plaque. *Quart. J. Geol. Soc.* **90**, ciiP.
1934–1935. The effect of incomplete diets on the concentration of ascorbic acid in the organs of rats. *Chem. Ind.* **53**, 874.
1935. The study of human nutrition: the outlook to-day. *J. Roy. Soc. Arts*, **83**, 572; *Brit. Med. J.* **1**, 571.
1935. Discovery and significance of vitamins. *Nature*, **135**, 708.
1935. The spirit of modern biochemistry. (A modern biochemia szelleme.) *Orvosi Hetilap*, **79**, 1045.
1935. Discovery and significance of vitamins. *Smithsonian Rep.* p. 265.
1935. Address of the President. Anniversary meeting, 30 November 1934. *Proc. Roy. Soc. A*, **148**, 1; *Proc. Roy. Soc. B*, **116**, 403.
1935. The ideals and realities of pharmacy. Inaugural address at the opening of the School of Pharmacy. *Pharmaceut. J.* **135**, 347.
1935. An experiment in first-class protein. (Introduction to a paper by H. C. Corry Mann.) *Lancet*, **1**, 145.
1935. (With B. R. Slater.) The effects of incomplete diet on the concentration of ascorbic acid in the organs of the rat. *Biochem. J.* **29**, 2803.
1935. Preparation of the pharmacist. *Lancet*, **2**, 797.
1936. Address of the President. Anniversary meeting, 30 November 1935. *Proc. Roy. Soc. A*, **153**, 247; *Proc. Roy. Soc. B*, **119**, 88.
1936. Sir Archibald Garrod. (Obituary notice.) *Brit. Med. J.* **1**, 775; *Nature, Lond.* **137**, 770.
1936. The naturalist in the laboratory. (Address of the Honorary President, London Natural History Society.) *Lond. Naturalist*, p. 40.
1936. (With E. J. Morgan.) Some relations between ascorbic acid and glutathione. *Biochem. J.* **30**, 1446.
1936. The influence of chemical thought on biology. *Science*, **84**, 255.
1936. The pace of science. (Foundation oration, Birkbeck College.) Birkbeck Coll. London.
1937. Memorial to Walter Morley Fletcher. Oxford Univ. Press. 13 pp.
1938. (With E. J. Morgan.) The influence of thiol-groups in the activity of dehydrogenases. *Biochem. J.* **32**, 611.
1938. Biological thought and chemical thought. A plea for unification. (Linacre lecture.) *Lancet*, **1**, 1147–1201.
1938. On lactoflavin as a sensitizer in the photocatalytic oxidation of ascorbic acid. *C. R. Trav. Lab. Carlsberg*, Ser. Chim. **22**, 226.
1938. (With E. M. Crook.) Further observations on the system ascorbic acid—glutathione—ascorbic acid-oxidase. *Biochem. J.* **32**, 1356.
1938. (With E. J. Morgan and C. Lutwak-Mann.) The influence of thiol groups in the activity of dehydrogenases. II. With an addendum on the location of dehydrogenases in muscle. *Biochem. J.* **32**, 1829.
1939. Importance of laboratory effort in cancer research. *Brit. Med. J.* **2**, 1.
1939. Justification of experimental investigation of cancer. *Med. Pr.* **201**, 609.
1939. (With C. Lutwak-Mann and E. J. Morgan.) Activity of the succinic dehydrogenase. *Nature*, **143**, 556.
1941. Inaugural address to Nutrition Society at Cambridge. *Proc. Nutr. Soc.* **1**, 3.
1942. A contribution to the chemistry of pterins. *Proc. Roy. Soc. B*, **130**, 359.
1942. (With C. J. Martin.) Arthur Harden, 1865–1940. *Roy. Soc. Obit. Notices*, **4**, 3.
1943. (With C. J. Martin.) Arthur Harden. (Obituary notice.) *J. Chem. Soc.* p. 334.
1943. (With E. J. Morgan.) The appearance of glutathione during the early stages of the germination of seeds. *Nature*, **152**, 288.

1944. (With I. Simon Reuss.) The effect of hypoxanthine on the growth of an avian tissue *in vitro*. *Proc. Roy. Soc. B*, **132**, 253.

1945. (With E. J. Morgan.) On the distribution of glyoxalase and glutathione. *Biochem. J.* **39**, 320.

1945. (With V. R. Leader.) On refection in rats and on the nature of the growth promoted by the addition of small quantities of milk to vitamin-free diets. *J. Hygiene, Camb.* **44**, 149.

1948. (With E. J. Morgan.) Studies on glyoxalase. I. A new factor. *Biochem. J.* **42**, 23.

PRINTED FOR THE ROYAL SOCIETY OF LONDON BY
MORRISON AND GIBB LTD., LONDON AND EDINBURGH